

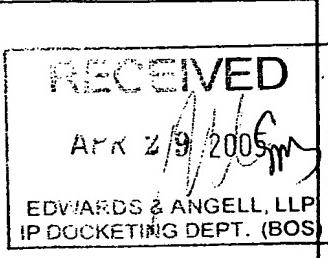
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54752 TWO (10 du)

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
 GREGORY B. BUTLER  
 EDWARDS & ANGELL, LLP  
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PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

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Applicant's or agent's file reference  59752-PCT		FOR FURTHER ACTION See paragraph 2 below	
International application No.  PCT/US04/33349	International filing date (day/month/year)  08 October 2004 (08.10.2004)	Priority date (day/month/year)  08 October 2003 (08.10.2003)	
International Patent Classification (IPC) or both national classification and IPC  IPC(7): C07D 207/06 and US Cl.: 548/571			
Applicant  PRESIDENT AND FELLOWS OF HARVARD COLLEGE			

## 1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

## 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

## 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US  Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer  Rebecca L. Anderson  Telephone No. (703) 308-1235
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Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/33349

**Box No. I Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- a sequence listing  
 table(s) related to the sequence listing

b. format of material

- in written format  
 in computer readable form

c. time of filing/furnishing

- contained in international application as filed.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority for the purposes of search.

3.  In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/33349

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application  
 claims Nos. 1-51 and 53-76

because:

- the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-51 and 53-76 are so unclear that no meaningful opinion could be formed (*specify*):

The numerous variables, e.g. R1, p, n, m, R2, R3, R4, X, Y, R', r, R'', etc., their voluminous complex meanings, their virtual incomprehensible permutations and combinations and the numerous proviso section make it impossible to determine the full scope and complete meaning of the claimed subject matter. As presented the claimed subject matter cannot be regarded as being a clear and concise description for which protection is sought and as such the listed claims do not comply with the requirements of PCT Article 6. Thus it is impossible to carry out a meaningful written opinion on same. A written opinion will be given on the first discernable invention which is the first three compounds of claim 52.

Furthermore, claims, 23-49 and 60-76 are improper multiple dependent claims under PCT Rule 6.4(a). Specifically, any dependent claim which refers to more than one other claim ("multiple dependent claim") shall refer to such claims in the alternative only. Multiple dependent claims shall not serve as a basis for any other multiple dependent claim.

- the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

- no international search report has been established for said claims Nos. \_\_\_\_\_

- the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- has not been furnished  
 does not comply with the standard  
 has not been furnished  
 does not comply with the standard

the computer readable form

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- See Supplemental Box for further details.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No. PCT/US04/33349
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**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims <u>52</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>52</u>	NO
Industrial applicability (IA)	Claims <u>52</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and explanations:**

Claim 52 lacks an inventive step under PCT Article 33(3) as being obvious over SEEGER (US Patent No. 3,287,217) SEEGER discloses the compounds of the formula (I) which are useful as pharmacodynamic compositions wherein R can be lower alkyl and halogen and R' can be alkyl with 2-8 carbon atoms. Furthermore, the SEEGER compound of example II differs only from applicants instantly claimed 4-methyl-2-pyrrolidin-1-yl-1 p-toylyl-pentan-1-one by the alkyl chain of R'. However, SEEGER et al, generically discloses 2-8 carbon atoms. Also, SEEGER compound VII differs only from applicants 1-(4-iodo-phenyl)-2-pyrrolidin-1-yl-pentan-1-one by the halogen substituent of R, of which it is considered obvious to modify one halogen atom for another, the basis of this reasoning is that chlorine and iodine are both halogen elements from the seventh group of the periodic system and the claimed compound is thus an analogue or an isologue of that disclosed in the prior art. The compounds are expected to possess similar properties differing only in degree.

Claim 52 meets the criteria set out in PCT Article 33(4), and thus has industrial applicability because the subject matter claimed can be made or used in industry.